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CARDIOMETABOLIC RISK FACTORS' PREVALENCE IN A POPULATION OF GERIATRICS WITH ELEVATED SERUM PROSTATE SPECIFIC ANTIGEN LEVELS

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ABSTRACT
Cardiometabolic, and prostatic, diseases are now recognized to be prevalent conditions even in our environment. This study seeks to estimate the prevalence of cardiometabolic risk factors in a population of geriatrics (age range: 65 – 84 years; self reported) with elevated serum prostate specific antigen levels – a marker of prostatic pathologies. Anthropometric indices, blood pressure values and relevant biochemical parameters were measured/determined, and their derivatives calculated using standard protocols and equations. Disease states/syndromes and (sub) phenotypes were defined based on internationally accepted methods. Hypertension, obesity and diabetes mellitus were found in 47.5%, 35% and 5%, respectively, of the population. A total of 52.5% of the population had hypertriglyceridemia, while 12.5% and 7.5% of the population had the hypertriglyceridemic waist phenotype and the metabolic syndrome respectively. As much as 25% and 20% of the subjects had values for the "lipid accumulation product" and the "visceral adiposity index", respectively that were higher than the normal threshold values. The "metabolically healthy obese" phenotype was found in 27.5% of the population while 7.5% of the population were found to be both metabolically and BMI-wise obese. The studied cardiometabolic risk factors were quite prevalent in this population. Management of prostatic diseases in Nigeria should include therapeutic approaches that target the reduction in morbidity due to these risk factors.

KEYWORDS: cardiometabolic risk factors, geriatrics, prevalence, prostatic diseases

INTRODUCTION

Prostate specific antigen (PSA) is a 33 kDa kallikren-like serine protease that is produced almost exclusively, and secreted, by the epithelial cells of the prostate. It is an organ-specific but not disease-specific protein as its concentration in serum increases as a result of any of the three major pathologies of the prostate – prostate cancer, benign prostatic hyperplasia and prostatitis. PSA titers are usually highest in cases of prostate cancer, moderately elevated in benign prostatic hyperplasia and least in prostatitis. Its concentration in serum is used as an index of disease progression and treatment outcomes (Chadha *et al.*, 2011).

Prostate cancer and benign prostatic hyperplasia are believed to be linked etiologically, since both result from an aberrant over-growth of prostatic cells; differing only in the fact that a carcinogen is required to initiate the former (Ejike and Ezeanyika, 2009). The pathogenesis of both diseases are thought to be centered around imbalances in sex hormones' metabolism and metabolic derangements that arise from the accumulation of cardiometabolic risk factors (Ejike and Ezeanyika, 2010). In fact, prostate cancer and benign prostatic hyperplasia have been linked to these metabolic abnormalities (Ejike and Ezeanyika, 2008; De Nunzio *et al.*, 2011; Zilli *et al.*, 2011).

Prostate cancer and benign prostatic hyperplasia are quite prevalent in Nigeria. A prostate cancer hospital incidence rate of 127 per 100,000 cases was reported for Lagos, by Osegbe (1997). A later study by Ogunbiyi and Shittu (1999) (from the Ibadan cancer registry) reported that 11% of all male cancers were of the prostate. Furthermore, Ukoli *et al.* (2003) reported that the proportion of men with PSA greater than or equal to 4 ng/mL (the threshold for the establishment of a diseased prostate) is comparable to that of previously unscreened populations with high incidence of prostate cancer such as African-American men. A prevalence of 25.35% for benign prostatic hyperplasia symptoms has been reported in Nsukka (Ezeanyika *et al.*, 2006). These figures are comparable to figures from industrialized nations. Just like prostatic diseases, cardiometabolic pathologies are also becoming prevalent in Nigeria (Ejike *et al.*, 2009; Ijeh *et al.*, 2010).

Unfortunately, there are no published studies (to our knowledge) on the prevalence of cardiometabolic risk factors in Nigerian men with elevated serum PSA levels, indicative of prostate cancer or benign prostatic hyperplasia. This study attempts to provide such data.

SUBJECTS AND METHODS

Subjects

Adult male Nigerians, living in and around Umuahia, aged 65 to 84 years, and attending the Out-Patient Urology Clinic at the Federal Medical Center Umuahia, Abia State, Nigeria were recruited for this study. Subjects who had any signs of overt morbidity were excluded from the study. Giving an informed oral consent was a prerequisite for participation in the study. Self reported age was recorded for each participant. Only data from subjects with PSA values ≥ 7.0 ng/ml were eventually analyzed. The study was designed in accordance with the Helsinki declaration. The Board of the Department of Biochemistry, Michael Okpara University of Agriculture, Umudike , and the Ethics committee of the Federal Medical Center Umuahia approved the design and methods for this study.

Methods

Anthropometry

Height (per participant) was measured to the nearest 0.1cm, with a measuring tape fastened to a vertical rod, and with the subject standing on bare feet. The waist circumference (WC) and hip circumference (HC) of each participant were also measured to the nearest 0.1cm, using a non-elastic measuring tape. WC was measured at minimal respiration, midway between the lowest rib and the superior border of the iliac crest while HC was measured at the widest circumference over the buttocks. Weight (for each subject) was measured to the nearest 0.1Kg using an electronic weighing balance. From these measurements, WHpR was calculated as WC/HC; WHtR was calculated as WC/Height; and BMI was calculated as Weight (Kg)/[Height $(m)^2$].

Blood pressure measurements

Participants had their blood pressures measured between 8am and 10am, using a mercury sphygmomanometer and appropriate cuff sizes. Each subject was required to have an initial ten minutes rest in a cool noiseless room. Three separate blood pressure measurements were taken with the subject seated, at five minutes intervals. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were taken at the 1^{st} and 5^{th} Korotkoff sounds respectively. The average of the second and third readings per subject was recorded, while the value for the first reading was discarded.

Biochemical Analysis

PSA concentration in serum was assayed for by the method of Kuriyama *et al.* (1980). Fasting blood glucose (FBG) levels were determined by the glucose oxidase method (Washako and Rice, 1961). Fasting circulating serum triacyglycerol (TAG), total cholesterol and HDL-C concentrations were measured using the enzymatic colorimetric methods of Lopes-Virella *et al.* (1977), Allain *et al.* (1974) and Tietz (1990) respectively. LDL-C was estimated by difference (Friedwald *et al.*, 1972).

Definitions and Derivations

Hypertension, obesity and diabetes were defined as SBP/DBP ≥ 140/90 mmHg (Giles *et al.*, 2009), BMI ≥ 30 kg/m^2 (WHO, 1995) and FBG level ≥ 126 mg/dl (WHO/IDF 2006) respectively. Subjects with a WC ≥ 94 cm and a fasting serum triacylglycerol concentration of ≥ 150 mg/dl were classified as having the hypertriglyceridemic waist phenotype; a modification of the Lemieux *et al.* (2000) classification. The metabolic syndrome was defined using the harmonized definition of Alberti *et al.*(2009). Lipid Accumulation Product was derived using the equation of Kahn (2005): LAP = (WC-65) × TAG. Visceral Adiposity Index was derived using the equation of Amato *et al.* (2010): VAI = [WC/39.68 + (1.88 × BMI)] × (TAG/1.03) × (1.31/HDL-C). The BMI-metabolic risk sub-phenotypes were defined according to the method used by Ijeh *et al.* (2010).

Statistical Analyses

Descriptive statistics were carried out on the continuous data generated (and their derivatives), and the results reported as means ± standard deviations. Categorical data were reported as percentages. All data analyses were done using SPSS (version 17.0) statistical software (SPSS Inc. Chicago, IL). The results are presented in a table and bar charts.

RESULTS

A total of forty subjects were studied. The clinical characteristics of the subjects are presented in Table 1. From Figure 1, it is seen that 47.5% of the population were hypertensive, while only 5% of the population were diabetic.

Table 1: Clinical characteristics of the subjects

Age (Yrs)	Weight (kg)	Height (m)	BMI (kg/m^2)	WC (cm)	HC (cm)	WHpR	WHtR	VAI
75.0±5.7	70.4±7.4	1.6±0.1	28.5±3.7	91±5	86±5	1.1±0.1	0.6±0.1	3.9±0.7
LAP	SBP (mmHg)	DBP (mmHg)	LDL (mg/dl)	HDL (mg/dl)	TChol (mg/dl)	TAG (mg/dl)	FBG (mg/dl)	PSA (ng/ml)
3959.7±730.2	123±26	72±14	10.8±8.4	49.6±6.2	90.7±10.9	151.4±15.3	87.3±20.7	22.0±3.1

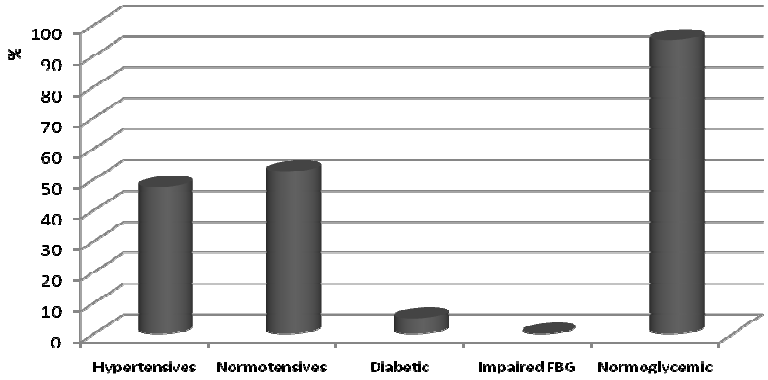

Fig. 1: Prevalence of hypertension and abnormal glucose metabolism in the population

Based on the BMI criteria, 35% of the subjects were obese, while 50% of the population were overweight (Fig. 2). Using the standard cut-off for WHpR and WHtR, as much as 100% and 90% of the population, respectively, had visceral obesity. However, using the cut-off values from our predictive equations (data not shown), 27.5% of the population had WHpR and WHtR that were predictive of cardiometabolic disorders (Fig.2). Figure 3 shows that 52.5% of the population had hypertriglyceridemia, while 12.5% of the subjects had the hypertriglyceridemic waist phenotype. Twenty five per cent and 20% of the population had abnormal LAP and VAI scores respectively (Fig.3).

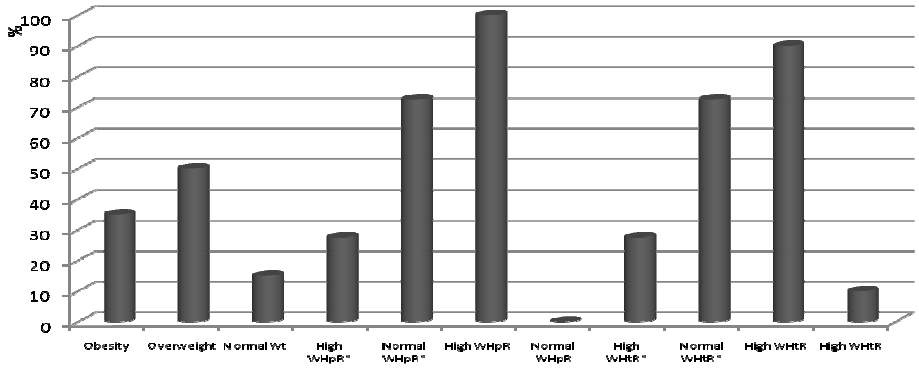

Fig.2: Prevalence of excess weight (by varying definitions) in the population
Wt, WHpR and WHtR represent weight, waist to hip ratio and waist to height ratio respectively.

The metabolic syndrome was found in 7.5% of the population, as is seen in Figure 4. A total of 27.5% of the population were metabolically healthy, but obese (by BMI standards) and none of the subjects was found to have the metabolically obese normal weight phenotype (Fig.4). Also, only 7.5% of the population were both metabolically and BMI-wise obese, whereas 65% of the population were metabolically healthy and alsp had normal weight BMI.

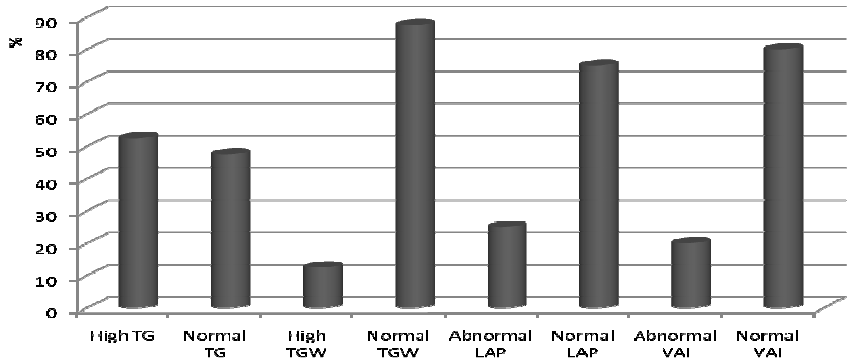

Fig.3: Prevalence of metabolic descriptors of cardiometabolic risk in the population
TG,TGW, LAP and VAI represent triacylglycerols, hypertriglyceridemic waist phenotype, lipid accumulation product and visceral adiposity index respectively

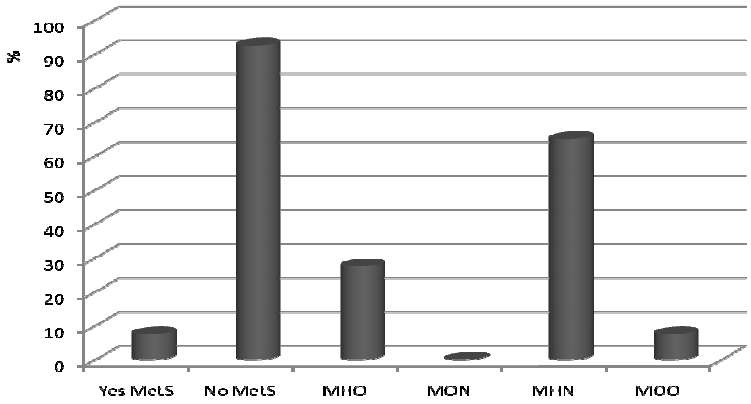

Fig.4: BMI-metabolic risk sub-phenotypes in the population
MetS, MHO, MON, MHN and MOO represent metabolic syndrome, metabolically healthy obese, metabolically obese normal weight and metabolically obese obese respectively.

DISCUSSION

Hypertension is a major public health concern, estimated to eventually affect as much as 1.56 billion people (60% of the world's population) by 2025 (Kearney *et al.,* 2005). In Nigeria the prevalence of hypertension has risen in the last three decades in both the adolescent and adult populations (Ejike *et al.,* 2010; Ulasi *et al.,* 2010). The finding that 47% of the studied population had hypertension shows that the prevalence of the disease in this geriatric population is higher than what is reported in the general adult Nigerian population (20-33%). It is however not surprising since hypertension prevalence is known to increase with age (Flack *et al.,* 2003) and has been shown to be associated with elevated plasma total cholesterol (Awusi and Onyeneke, 2009) and prostatic endocrine-related diseases (Wallner *et al.,* 2011). The 5% prevalence of diabetes found in this population is higher than the 2-2.5% reported earlier in Nigeria (Dahiru *et al.,* 2008). Again diabetes mellitus and impaired glucose metabolism are important components of the metabolic syndrome and have been linked to prostatic diseases (Abdollah *et al.,* 2011).

Obesity was found to be particularly prevalent in the studied population. This is more so when the standard cut-off values for WHpR and WHtR (<1 and <0.5 respectively) are used, and virtually all the subjects appear to have excess visceral mass. However, because the inherent disadvantages of using anthropometry in assessing

metabolic risks, we had earlier estimated cut-off points for WHpR and WHtR that predict cardiometabolic risks for this population, using appropriate statistical methods (author's unpublished data). The 27.5% prevalence of visceral obesity/adiposity in this population is high especially given the fact that the visceral adipose tissue is the site for the storage of ectopic fat which is a major culprit in conferring cardiometabolic risk. In fact, WHpR and WHtR perform better than BMI in predicting cardiovascular disease (CVD) risk (Lee *et al.,* 2008; Huxley *et al.,* 2010) and both have been associated with prostatic disorders (De Nunzio *et al.,* 2011).

LAP is a simple index for estimating lipid over accumulation in adults (Kahn, 2005), while VAI also expresses visceral fat function (Amato *et al.,* 2010). Both LAP and VAI therefore capture the contexts in which excessive lipid accumulation could result in physiological dangers. Again, like LAP and VAI, the cardiometabolic waist phenotype describes individuals with elevated circulating serum triacylglycerols and a concomitant excess waist circumference, and therefore with heightened cardiometabolic risks. It is therefore worrisome (but not unexpected) that as much as 25% and 20% of this geriatric population have higher than normal values for LAP and VAI respectively; while 12.5% had the hypertriglyceridemic waist phenotype. These findings (and the high prevalence of hypertriglyceridemia in the population, 52.5%) are not unexpected because lipid over accumulation is a principal factor is the sequence of events that lead to the metabolic syndrome, and prostatic diseases (at least BPH) are thought to be a component of the metabolic syndrome (Harmmarsten and Peeker, 2011).

The metabolic syndrome was found in 7.5% of the entire population who also were obese by BMI standards. However, 27.5% of the population were obese by BMI standards, but were found to be metabolically healthy. The prevalence of BMI-metabolic risk phenotypes has been reported in Nigeria (Ejike *et al.,* 2009; Ijeh *et al.,* 2010). These phenotypes distinguish obesity from its usual metabolic consequences as seen in "metabolically obese normal weight" individuals, or risks that are associated with obesity that are independent of adiposity as seen in metabolically healthy obese individuals (Ejike *et al.,* 2009). As much as 35% of the studied population had either the metabolic syndrome or BMI-wise obesity. Again given the established relationship between prostate cancer and benign prostatic hyperplasia on the one hand, and metabolic derangements on the other hand, these prevalence figures though high, still are within expected regions for a population like the one we studied.

This study is limited by its small sample size. However given the specific nature of the study design, and the low life expectancy of Nigerian males, the sample size should suffice to serve as motivation for further studies on similar populations across Nigeria and beyond. Certain religious and cultural belief systems dominant in these parts also make it particularly difficult to convince people to part with their blood, especially when a 'stranger' makes the demand. This study is nonetheless robust in its design and analysis and reports (for the first time) the prevalence of factors that are thought to be driving (at least in part) the rising prevalence of prostate cancer and benign prostatic hyperplasia, globally and locally.

CONCLUSION

Cardiometabolic risk factors are very prevalent in this population of geriatrics with elevated serum PSA levels. The high prevalence of these risk factors in this population is in tandem with reports of associations between these risk factors and prostatic diseases. Management of prostatic diseases should incorporate pharmacological therapy and lifestyle modifications targeted at reducing the levels of these cardiometabolic risk factors in the population.

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